Amendments to the Claims

I. Amendments

Please withdraw claims 1-4 and 56-95, without prejudice or disclaimer, as directed to non-elected inventions.

Please cancel claims 15, and 21-22, without prejudice or disclaimer to the subject matter claimed therein.

II. The Claims of the Application

Claim 1 (**Withdrawn**): A method for enhancing the uptake of a molecule into a metabolically active whole cell, comprising incubating said metabolically active whole cell with said molecule in the presence of an agent that causes increased uptake of molecules into metabolically active cells, said agent being present at a concentration sufficient to enhance the uptake of said substrate or analyte compound into said metabolically active whole cell.

Claim 2 (**Withdrawn**): The method of claim 1, wherein said agent that causes increased uptake of molecules into metabolically active cells is selected from the group consisting of glycerol, dimethyl sulfoxide (DMSO), trehalose, glutamate, betaine, ethylene glycol, threitol, ribose, and trimethylamine N-oxide.

Claim 3 (**Withdrawn**): The method of claim 1, wherein said molecule permits the staining, imaging or visualization of said cell or of structures, regions or molecules within said cell.

Claim 4 (**Withdrawn**): The method of claim 1, wherein said molecule is selected from the group consisting of a lectin, a nucleic acid, a paramagnetic moiety, an enzyme substrate or an analyte.

Claim 5 (**Currently Amended**): A method for assaying **a metabolically active whole cell** for the presence or activity of an enzyme ~~**in a metabolically active whole cell**~~, comprising the steps:

(a) incubating said metabolically active whole cell with a substrate of said enzyme or an analyte compound in the presence of an agent that enhances uptake of said substrate or analyte, said agent being present at a concentration sufficient to enhance the uptake of said substrate or analyte compound;

(b) assaying **said metabolically active whole cell** for any change in concentration of said substrate or analyte compound or of a product formed via action of said enzyme on said substrate or analyte;

wherein a change in said concentration is indicative of the presence or activity of said enzyme in said metabolically active whole cell**; and**

wherein said agent that enhances uptake of said substrate or analyte is selected from the group consisting of glycerol, dimethyl sulfoxide (DMSO), trehalose, glutamate, betaine, ethylene glycol, threitol, ribose, and trimethylamine N-oxide, with the proviso that when said agent is dimethyl sulfoxide (DMSO), said agent will be present at a concentration of between about 20% and about 60% (v/v).

Claim 6 (**Original**): The method of claim 5, wherein said enzyme is selected from the group consisting of a 5' nucleotidase, acetylcholinesterase, an acid phosphatase, an acidic esterase, an acidic esterase I, an acidic esterase II, an acidic non-specific esterase, an adenosine deaminase, an adenosine monophosphate deaminase, an alkaline phosphatase, an aminopeptidase A, an aminopeptidase B, an aminopeptidase M, an Aminopeptidase N, an angiotensin converting enzyme, a caspase, a cathepsin B, a cathepsin B1, a cathepsin C, a cathepsin D, a cathepsin H, a cathepsin L, a cholinesterase, a cholinesterase, a chymotrypsin, a collagenase, a cytosine deaminase, a DPP I, a DPP II, a DPP IV, an elastase,

an endopeptidase I, an endopeptidase II, an ester proteinase, a galactopyranosidase, a glucoronidase, a glutathione, a glycopyranossidase, a guanine deaminase, an HIV Protease, a lipase, a membrane associated endopeptidase I, a membrane associated endopeptidase II, a neutral endopeptidase, a neutral esterase, a neutral esterase I, a neutral esterase II, a neutral non-specific esterase, a nucleosidase, a pancreatin, a phospholipase A, a phospholipase C, a phospholipase D, a plasmin, a serine phosphatase, a tartrate resistant phosphatase, a tartrate resistant phosphatase, a threonine phosphatase, a thymidine deaminase, a tripeptidyl peptidase, a trypsin, a tyrosine phosphatase, a urokinase, a v-thrompsin, and a γ-GT.

Claim 7 (**Original**): The method of claim 6, wherein said enzyme is a caspase.

Claim 8 (**Original**): The method of claim 7, wherein said caspase is caspase 1, caspase 3, caspase 6, caspase 8 or caspase 9.

Claim 9 (**Original**): The method of claim 5, wherein said substrate or analyte compound of said enzyme and said agent that enhances uptake are mixed during said incubation.

Claim 10 (**Original**): The method of claim 5, wherein said substrate or analyte compound of said enzyme and said agent that enhances uptake are not mixed during said incubation.

Claim 11 (**Original**): The method of claim 5, wherein multiple enzymes are assayed simultaneously assayed.

Claim 12 (**Original**): The method of claim 5, wherein multiple enzymes are sequentially assayed.

Claim 13 (**Currently Amended**): The method of claim 5, wherein said substrate or analyte compound comprises ~~**comprising**~~ an indicator group and one or more

leaving groups, each of said leaving groups being selected for cleavage by said enzyme, said indicator group being in a first state when bonded to a leaving group, and being in a second state when said leaving group is cleaved from said indicator group by said enzyme; and wherein said step (b): comprises sensing whether said second state of said indicator group is produced; wherein the production of said second state of said indicator group is indicative of the presence or activity of said enzyme in said metabolically active whole cell.

Claim 14 (**Original**): The method of claim 13, wherein said indicator group is a fluorescent, colorimetric, bioluminescent or chemiluminescent indicator group.

Claim 15 (**Cancelled**)

Claim 16 (**Currently Amended**): The method of **claim 5**, wherein said uptake-enhancing agent is glycerol.

Claim 17 (**Original**): The method of claim 16, wherein said glycerol concentration is between about 5% and about 60% (v/v).

Claim 18 (**Original**): The method of claim 17, wherein said glycerol concentration is between about 20% and about 60% (v/v).

Claim 19 (**Original**): The method of claim 18, wherein said glycerol concentration is between about 25% and about 40% (v/v).

Claim 20 (**Currently Amended**): The method of **claim 5**, wherein said uptake-enhancing agent is dimethyl sulfoxide (DMSO).

Claim 21 (**Cancelled**)

Claim 22 (**Cancelled**)

Claim 23 (**Currently Amended**): The method of **claim 5**, wherein said uptake-enhancing agent is glutamate.

Claim 24 (**Currently Amended**): The method of claim 23, wherein said glutamate concentration is between about 0.25 M and ~~**about 2.0 M**~~ **about 2 M**.

Claim 25 (**Original**): The method of claim 24, wherein said glutamate concentration is between about 1 M and about 2 M.

Claim 26 (**Currently Amended**): The method of **claim 5**, wherein said uptake-enhancing agent is betaine.

Claim 27 (**Original**): The method of claim 26, wherein said betaine concentration is about 0.3 M or greater.

Claim 28 (**Currently Amended**): The method of **claim 5**, wherein said uptake-enhancing agent is trehalose.

Claim 29 (**Original**): The method of claim 28, wherein said trehalose concentration is between about 0.1 M and about 1.5 M.

Claim 30 (**Currently Amended**): The method of **claim 5**, wherein said uptake-enhancing agent is ethylene glycol.

Claim 31 (**Original**): The method of claim 30, wherein said ethylene glycol concentration is between about 2 M and about 7 M.

Claim 32 (**Currently Amended**): The method of **claim 5**, wherein said uptake-enhancing agent is threitol.

Claim 33 (**Original**): The method of claim 32, wherein said threitol concentration is between about 1 M and about 5 M.

Claim 34 (**Currently Amended**): The method of **claim 5**, wherein said uptake-enhancing agent is ribose.

Claim 35 (**Original**): The method of claim 34, wherein said ribose concentration is between about 0.4 M and about 4 M.

Claim 36 (**Currently Amended**): The method of **claim 5**, wherein said uptake-enhancing agent is triethylamine N-oxide.

Claim 37 (**Original**): The method of claim 36, wherein said triethylamine N-oxide concentration is between about 0.4 M and about 4 M.

Claim 38 (**Original**): The method of claim 13, wherein said enzyme is selected from the group consisting of a 5' nucleotidase, acetylcholinesterase, an acid phosphatase, an acidic esterase, an acidic esterase I, an acidic esterase II, an acidic non-specific esterase, an adenosine deaminase, an adenosine monophosphate deaminase, an alkaline phosphatase, an aminopeptidase A, an aminopeptidase B, an aminopeptidase M, an Aminopeptidase N, an angiotensin converting enzyme, a caspase, a cathepsin B, a cathepsin B1, a cathepsin C, a cathepsin D, a cathepsin H, a cathepsin L, a cholinesterase, a cholinesterase, a chymotrypsin, a collagenase, a cytosine deaminase, a DPP I, a DPP II, a DPP IV, an elastase, an endopeptidase I, an endopeptidase II, an ester proteinase, a galactopyranosidase, a glucoronidase, a glutathione, a glycopyranossidase, a guanine deaminase, an HIV Protease, a lipase, a membrane associated endopeptidase I, a membrane associated endopeptidase II, a neutral endopeptidase, a neutral esterase, a neutral esterase I, a neutral esterase II, a neutral non-specific esterase, a nucleosidase, a pancreatin, a phospholipase A, a phospholipase C, a phospholipase D, a plasmin, a serine phosphatase, a tartrate resistant phosphatase, a tartrate resistant phosphatase, a threonine phosphatase,

a thymidine deaminase, a tripeptidyl peptidase, a trypsin, a tyrosine phosphatase, a urokinase, a v-thrompsin, and a γ-GT.

Claim 39 (**Original**): The method of claim 38, wherein said enzyme is a caspase.

Claim 40 (**Original**): The method of claim 39, wherein said caspase is caspase 1, caspase 3, caspase 6, caspase 8, or caspase 9.

Claim 41 (**Original**): The method of claim 13, wherein multiple enzymes are simultaneously assayed.

Claim 42 (**Original**): The method of claim 13, wherein multiple enzymes are sequentially assayed.

Claim 43 (**Original**): The method of claim 13, wherein said step (b) includes measuring an intensity of said second state against time.

Claim 44 (**Original**): The method of claim 13, wherein said step (b) includes measuring a magnitude of said second state at a point of time.

Claim 45 (**Original**): The method of claim 13, wherein said substrate or analyte compound comprises more than one leaving group, and wherein each of said substrate's leaving groups is cleaved sequentially by said enzyme.

Claim 46 (**Original**): The method of claim 13, wherein said indicator group is selected from the group consisting of rhodamine 110, rhodol, fluorescein, coumarin, and derivatives thereof.

Claim 47 (**Original**): The method of claim 46, wherein said derivatives of rhodamine 110, rhodol, fluorescein and coumarin are selected from the group consisting of 4'(5')thiofluorescein, 4'(5')-aminofluorescein, 4'(5')-carboxyfluorescein, 4'(5')-chlorofluorescein, 4'(5')-methylfluorescein, 4'(5')-sulfofluorescein, 4'(5')-

aminorhodol, 4'(5')-carboxyrhodol, 4'(5')-chlororhodol, 4'(5')-methylrhodol, 4'(5')-sulforhodol; 4'(5')-aminorhodamine 110, 4'(5')-sulforhodamine 110, 4'(5')thiorhodamine 110, 7-aminocoumarin, and sulfonated coumarin.

Claim 48 (**Original**): The method of claim 13, wherein said assay detects the presence or absence of an abnormality in the activity of said enzyme by comparing the production of said second state of said indicator group by said test cell to the production of said second state of said indicator group by a reference normal cell.

Claim 49 (**Original**): The method of claim 48, wherein said abnormality is a morphological or disease state.

Claim 50 (**Original**): The method of claim 49, wherein said morphological state is an apoptotic state.

Claim 51 (**Original**): The method of claim 49, wherein said disease state is a tumorigenic state.

Claim 52 (**Original**): The method of claim 13, wherein said substrate or analyte compound contains a blocking group.

Claim 53 (**Original**): The method of claim 52, wherein said blocking group is a Cbz blocking group.

Claim 54 (**Original**): The method of claim 13, wherein said substrate or analyte compound of said enzyme and said agent that enhances said uptake are mixed during said incubation.

Claim 55 (**Original**): The method of claim 13, wherein said substrate or analyte compound of said enzyme and said agent that enhances said uptake are not mixed during said incubation.

Claim 56 (**Withdrawn**): A reagent for assaying the activity of an enzyme, said reagent comprising a substrate of said enzyme or an analyte compound and an agent that enhances said uptake, said agent being present at a concentration sufficient to enhance the uptake of said substrate or analyte compound in a metabolically active cell.

Claim 57 (**Withdrawn**): The reagent of claim 56, wherein said enzyme is selected from the group consisting of a 5' nucleotidase, acetylcholinesterase, an acid phosphatase, an acidic esterase, an acidic esterase I, an acidic esterase II, an acidic non-specific esterase, an adenosine deaminase, an adenosine monophosphate deaminase, an alkaline phosphatase, an aminopeptidase A, an aminopeptidase B, an aminopeptidase M, an Aminopeptidase N, an angiotensin converting enzyme, a caspase, a cathepsin B, a cathepsin B1, a cathepsin C, a cathepsin D, a cathepsin H, a cathepsin L, a cholinesterase, a cholinesterase, a chymotrypsin, a collagenase, a cytosine deaminase, a DPP I, a DPP II, a DPP IV, an elastase, an endopeptidase I, an endopeptidase II, an ester proteinase, a galactopyranosidase, a glucoronidase, a glutathione, a glycopyranossidase, a guanine deaminase, an HIV Protease, a lipase, a membrane associated endopeptidase I, a membrane associated endopeptidase II, a neutral endopeptidase, a neutral esterase, a neutral esterase I, a neutral esterase II, a neutral non-specific esterase, a nucleosidase, a pancreatin, a phospholipase A, a phospholipase C, a phospholipase D, a plasmin, a serine phosphatase, a tartrate resistant phosphatase, a tartrate resistant phosphatase, a threonine phosphatase, a thymidine deaminase, a tripeptidyl peptidase, a trypsin, a tyrosine phosphatase, a urokinase, a v-thrompsin, and a γ-GT.

Claim 58 (**Withdrawn**): The reagent of claim 57, wherein said enzyme is a caspase.

Claim 59 (**Withdrawn**): The reagent of claim 58, wherein said caspase is caspase 1, caspase 3, caspase 6, caspase 8 or caspase 9.

Claim 60 (**Withdrawn**): The reagent of claim 56, wherein said substrate or analyte compound comprises comprising an indicator group and one or more leaving groups, each of said leaving groups being selected for cleavage by said enzyme, said indicator group being in a first state when bonded to a leaving group, and being in a second state when said leaving group is cleaved from said indicator group by said enzyme; and wherein said step (b): comprises sensing whether said second state of said indicator group is produced; wherein the production of said second state of said indicator group is indicative of the presence or activity of said enzyme in said metabolically active whole cell.

Claim 61 (**Withdrawn**): The reagent of claim 60, wherein said indicator group is a fluorescent, colorimetric, bioluminescent or chemiluminescent indicator group.

Claim 62 (**Withdrawn**): The reagent of claim 61, wherein said indicator group is a fluorescent or chemiluminescent indicator group.

Claim 63 (**Withdrawn**): The reagent of claim 56 or claim 61, wherein said uptake-enhancing agent is selected from the group consisting of glycerol, dimethyl sulfoxide (DMSO), trehalose, glutamate, betaine, ethylene glycol, threitol, ribose, and trimethylamine N-oxide.

Claim 64 (**Withdrawn**): The reagent of claim 63, wherein said uptake-enhancing agent is glycerol.

Claim 65 (**Withdrawn**): The reagent of claim 64, wherein said glycerol concentration is between about 5% and about 60% (v/v).

Claim 66 (**Withdrawn**): The reagent of claim 65, wherein said glycerol concentration is between about 20% and about 60% (v/v).

Claim 67 (**Withdrawn**): The reagent of claim 66, wherein said glycerol concentration is between about 25% and about 40% (v/v).

Claim 68 (**Withdrawn**): The reagent of claim 63, wherein said uptake-enhancing agent is dimethyl sulfoxide (DMSO).

Claim 69 (**Withdrawn**): The reagent of claim 68, wherein said dimethyl sulfoxide concentration is between about 5% and about 60% (v/v).

Claim 70 (**Withdrawn**): The reagent of claim 69, wherein said dimethyl sulfoxide concentration is between about 20% and about 60% (v/v).

Claim 71 (**Withdrawn**): The reagent of claim 63, wherein said uptake-enhancing agent is glutamate.

Claim 72 (**Withdrawn**): The reagent of claim 71, wherein said glutamate concentration is between about 0.25 M and about 2.0 M.

Claim 73 (**Withdrawn**): The reagent of claim 72, wherein said glutamate concentration is between about 1 M and about 2 M.

Claim 74 (**Withdrawn**): The reagent of claim 63, wherein said uptake-enhancing agent is betaine.

Claim 75 (**Withdrawn**): The reagent of claim 74, wherein said betaine concentration is about 0.3 M or greater.

Claim 76 (**Withdrawn**): The reagent of claim 63, wherein said uptake-enhancing agent is trehalose.

Claim 77 (**Withdrawn**): The reagent of claim 76, wherein said trehalose concentration is between about 0.1 M and about 1.5 M.

Claim 78 (**Withdrawn**): The reagent of claim 63, wherein said uptake-enhancing agent is ethylene glycol.

Claim 79 (**Withdrawn**): The reagent of claim 78, wherein said ethylene glycol concentration is between about 2 M and about 7 M.

Claim 80 (**Withdrawn**): The reagent of claim 63, wherein said uptake-enhancing agent is threitol.

Claim 81 (**Withdrawn**): The reagent of claim 80, wherein said threitol concentration is between about 1 M and about 5 M.

Claim 82 (**Withdrawn**): The reagent of claim 63, wherein said uptake-enhancing agent is ribose.

Claim 83 (**Withdrawn**): The reagent of claim 82, wherein said ribose concentration is between about 0.4 M and about 4 M.

Claim 84 (**Withdrawn**): The reagent of claim 63, wherein said uptake-enhancing agent is triethylamine N-oxide.

Claim 85 (**Withdrawn**): The reagent of claim 84, wherein said triethylamine N-oxide concentration is between about 0.4 M and about 4 M.

Claim 86 (**Withdrawn**): The reagent of claim 61, wherein said enzyme is selected from the group consisting of a 5' nucleotidase, acetylcholinesterase, an acid phosphatase, an acidic esterase, an acidic esterase I, an acidic esterase II, an acidic non-specific esterase, an adenosine deaminase, an adenosine monophosphate deaminase, an alkaline phosphatase, an aminopeptidase A, an aminopeptidase B, an aminopeptidase M, an Aminopeptidase N, an angiotensin converting enzyme, a caspase, a cathepsin B, a cathepsin B1, a cathepsin C, a cathepsin D, a cathepsin H, a cathepsin L, a cholinesterase, a cholinesterase, a chymotrypsin, a collagenase, a cytosine deaminase, a DPP I, a DPP II, a DPP IV, an elastase, an endopeptidase I, an endopeptidase II, an ester proteinase, a galactopyranosidase, a glucoronidase, a glutathione, a glycopyranossidase, a

guanine deaminase, an HIV Protease, a lipase, a membrane associated endopeptidase I, a membrane associated endopeptidase II, a neutral endopeptidase, a neutral esterase, a neutral esterase I, a neutral esterase II, a neutral non-specific esterase, a nucleosidase, a pancreatin, a phospholipase A, a phospholipase C, a phospholipase D, a plasmin, a serine phosphatase, a tartrate resistant phosphatase, a tartrate resistant phosphatase, a threonine phosphatase, a thymidine deaminase, a tripeptidyl peptidase, a trypsin, a tyrosine phosphatase, a urokinase, a v-thrompsin, and a γ-GT.

Claim 87 (**Withdrawn**): The reagent of claim 62, wherein said substrate or analyte compound comprises more than one leaving group, and wherein each of said substrate's leaving groups is cleaved consecutively by said enzyme to ultimately yield a free dye.

Claim 88 (**Withdrawn**): The reagent of claim 62, wherein said indicator group is selected from the group consisting of rhodamine 110, rhodol, fluorescein, coumarin, and derivatives thereof.

Claim 89 (**Withdrawn**): The reagent of claim 88, wherein said derivatives of rhodamine 110, rhodol, fluorescein and coumarin are selected from the group consisting of 4'(5')thiofluorescein, 4'(5')-aminofluorescein, 4'(5')-carboxyfluorescein, 4'(5')-chlorofluorescein, 4'(5')-methylfluorescein, 4'(5')-sulfofluorescein, 4'(5')-aminorhodol, 4'(5')-carboxyrhodol, 4'(5')-chlororhodol, 4'(5')-methylrhodol, 4'(5')-sulforhodol; 4'(5')-aminorhodamine 110, 4'(5')-sulforhodamine 110, 4'(5')thiorhodamine 110, 7-aminocoumarin, and sulfonated coumarin.

Claim 90 (**Withdrawn**): The reagent of claim 61, wherein said assay detects the presence or absence of an abnormality in the activity of said enzyme by comparing the production of said second state of said indicator group by said test cell to the

production of said second state of said indicator group by a reference normal cell.

Claim 91 (**Withdrawn**): The reagent of claim 90, wherein said abnormality is a morphological or disease state.

Claim 92 (**Withdrawn**): The reagent of claim 91, wherein said morphological state is an apoptotic state.

Claim 93 (**Withdrawn**): The reagent of claim 91, wherein said disease state is a tumorigenic state.

Claim 94 (**Withdrawn**): The reagent of claim 61, wherein said substrate or analyte compound contains a blocking group.

Claim 95 (**Withdrawn**): The reagent of claim 94, wherein said blocking group is a Cbz blocking group.